DOCKET NO.: ISIS-5031 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Phillip Dan Cook

Serial No.: **Not Yet Assigned** Group Art Unit: **Not Yet Assigned**

Filed: **Herewith** Examiner: **Not Yet Assigned**

For: **NUCLEOBASE HETEROCYCLIC COMBINATORIALIZATION**

EXPRESS MAIL INFORMATION

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DATE OF DEPOSIT: March 1, 2002

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

PRELIMINARY AMENDMENT

Prior to examination on the merits, Applicant respectfully requests that the application be amended as follows.

In the Specification:

Please insert the following paragraph beginning at page 1, between the title at line 1 and the section titled "FIELD OF THE INVENTION" at line 3 of the specification:

--CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of Application Serial No. 09/076,983 filed May 13, 1998, which is a divisional of Application Serial No. 08/884,873 filed June 30, 1997, each of which is incorporated herein by reference in its entirety.--

In the Claims:

Please cancel claims 1-30 and add new claims 31-50 as follows.

31. (New claim) A method for preparing a library of compounds comprising:

contacting a purine or pyrimidine heterocyclic scaffold having at least two functionalizable atoms, wherein at least one of said functionalizable atoms is blocked, with a mixture of at least six different chemical substituents to append each of said chemical substituents to said heterocyclic scaffold directly to form a substituent-appended scaffold;

deblocking at least one of said blocked functionalizable atoms of said substituent-appended scaffold; and

contacting said substituent-appended scaffold with a mixture of at least six different chemical substituents to append each of said chemical substituents to said substituent-appended scaffold either directly or via a tether moiety covalently attached to one of said functionalizable atoms.

32. (New claim) The method of claim 31 wherein said compounds of said library are within 20 mole percent of equimolarity.

33. (New claim) The method of claim 31 wherein said contacting steps are carried out in one reaction vessel.

34. (New claim) The method of claim 31 wherein said purine or pyrimidine is substituted or unsubstituted adenine, guanine, cytosine, uridine, thymine, xanthine or hypoxanthine.

35. (New claim) The method of claim 31 wherein said scaffold is contacted with a mixture of at least ten different chemical substituents.

36. (New claim) The method of claim 31 wherein said scaffold is contacted with a mixture of at least fifteen different chemical substituents.

37. (New claim) The method of claim 31 wherein said method is performed in solution phase.

38. (New claim) A method for preparing a library of compounds comprising:

contacting a purine or pyrimidine heterocyclic scaffold having at least two functionalizable atoms, wherein at least one of said functionalizable atoms is blocked, with a mixture of at least six different chemical substituents to append each of said chemical substituents to said heterocyclic scaffold via a tether moiety covalently attached to one of said functionalizable atoms to form a substituent-appended scaffold;

deblocking at least one of said blocked functionalizable atoms of said substituent-appended scaffold; and

contacting said substituent-appended scaffold with a mixture of at least six different chemical substituents to append each of said chemical substituents to said substituent-appended scaffold either directly or via a tether moiety covalently attached to one of said functionalizable atoms.

39. (New claim) The method of claim 38 wherein said compounds of said library are within 20 mole percent of equimolarity.

40. (New claim) The method of claim 38 wherein said contacting steps are carried out in one reaction vessel.

41. (New claim) The method of claim 38 wherein said purine or pyrimidine is substituted or unsubstituted adenine, guanine, cytosine, uridine, thymine, xanthine or hypoxanthine.

42. (New claim) The method of claim 38 wherein said scaffold is contacted with a mixture of at least ten different chemical substituents.

43. (New claim) The method of claim 38 wherein said scaffold is contacted with a mixture of at least fifteen different chemical substituents.

44. (New claim) The method of claim 38 wherein said method is performed in solution phase.

45. (New claim) A method for preparing a library of compounds comprising:

contacting a purine or pyrimidine heterocyclic scaffold molecule having a plurality of functionalizable atoms with a mixture of at least six different chemical substituents in one reaction vessel to append each of said chemical substituents to said scaffold either directly or via a tether moiety covalently attached to one of said functionalizable atoms.

46. (New claim) The method of claim 45 wherein said compounds of said library are within 20 mole percent of equimolarity.

47. (New claim) The method of claim 45 wherein said purine or pyrimidine is substituted or unsubstituted adenine, guanine, cytosine, uridine, thymine, xanthine or hypoxanthine.

48. (New claim) The method of claim 45 wherein said scaffold is contacted with a mixture of at least ten different chemical substituents.

49. (New claim) The method of claim 45 wherein said scaffold is contacted with a mixture of at least fifteen different chemical substituents.

50. (New claim) The method of claim 45 wherein saidmethod is performed in solution phase.

REMARKS

Claims 31-50 are pending in the present application. Applicant respectfully submits that the claims are in condition for allowance. An early notice of the same is earnestly solicited. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment.

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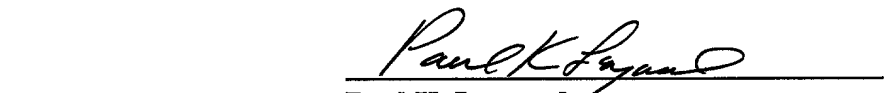
The attached page is captioned **"Version with markings to show changes made."**

Respectfully submitted,



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Date: **March 1, 2002**

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 1-30 have been cancelled.

New claims 31-50 have been added.